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EDITORIAL.

The Preparation of Medical Papers.

On reading medical literature one is struck by the great diversity of method used in the writing of papers. Some are written in the literary style of Osler; others are thrown together in a haphazard or incomplete way, with the result that excellent material is spoiled because the reader cannot follow the writer's argument. By following certain rules and by practice the craft of writing may be acquired.

The first consideration is the choice of a subject, and this must be made with care. If the writer cannot report original work he should at least choose a subject on which work has been done recently and which has not been completely summarized already. Also he must consider the type of journal in which the paper is to be published and choose a subject which will be of both interest and value to the readers of that journal, or, more logically, it may be done the other way—a subject chosen and then a suitable journal found.

Having decided on the subject the next step is to gather the material. This must be complete, as nothing chagrines an author more than to find that an important source of information has been overlooked. The surest method is to use the Index Medicus, make notes of all pertinent articles and then read them, making a summary of each. This brings a large amount of material into readily accessible form.

The presentation is quite as important as the material itself. An outline must be made and then followed. First comes the introduction; it should be brief, and it is better to avoid time-worn phrases. All the facts should then be

listed in logical order and divided and subdivided under suitable headings. The manner of division varies with different subjects, but, as a rule, that found in the standard text-books is satisfactory. Having presented the facts, the conclusions to which they lead are set down. At times the reader is left to draw his own conclusions but that gives a lack of finish to the paper and does not impress the reader as does one in which the writer takes a definite stand.

A summary, placed at the end, is a distinct asset to any scientific paper as it brings once more to the reader's attention the important points and he is able to quickly review the whole thing in his mind. Also if at any time he wishes to refresh his memory he may do so by simply reading the summary.

No one paper can give a complete account of all the literature on any subject, but should mention the work which has been done and its result, and in that way stimulate a desire for further reading. If an accurate list of references is attached, this further reading is greatly simplified and the author will have the blessing of his readers. Equally as important is the courtesy to the authors who have supplied the material for the paper.

After the paper has been written it is well to lay it aside for a considerable length of time and then look it over with a critical eye and ask oneself certain questions. Are the facts in logical order? Do the conclusions follow from the facts? Are there any unnecessary words or sentences? Is the list of references accurate? These and other questions should be considered in as disinterested a manner as possible, and then the paper rewritten.

The above is a brief outline. For greater detail a handbook on the subject may be consulted, such as "The Writing of Medical Papers" by Mellish.

The Differential Diagnosis of Clinical Conditions Accompanied by Jaundice.*

By DUNCAN GRAHAM, M.B.,
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Jaundice is the term applied to clinical conditions in which the tissues, sclera, mucous membranes and skin are stained yellow by bile pigment. That this deposit of bile pigment in the tissues occurs in a variety of conditions associated with diseases of the liver and biliary passages, and in certain forms of anaemia, has been known and recognized by clinicians for a long time. On the other hand, the accurate diagnosis of the disease condition responsible for the development of jaundice in different cases has been only too often difficult or impossible. This has been due chiefly to our lack of precise knowledge of the physiology of bile pigment formation. However, the discovery of a suitable method for the estimation of bile pigment in the blood, recent investigations of the site of bile pigment formation, and the relationship of the liver to bile pigment metabolism, both in health and disease, have given us a new theory of the mechanism of jaundice, and a new classification of its clinical varieties, which are proving of the greatest value in the diagnosis of conditions accompanied by jaundice.

Bile pigment is derived from hæmoglobin. The older view that this transformation occurs in the hepatic cells

*Reprinted from the Canadian Medical Association Journal, October, 1929. It is a paper read at the Sixteenth Annual Meeting of the Canadian Medical Association, June 19th, 1929.

must be discarded. In the light of recent investigations it may be stated that the bile pigment, bilirubin, is formed in the endothelial cells belonging to the reticulo-endothelial system. These cells, which are found chiefly in the spleen and bone marrow, and to a lesser extent in the liver (as the Kupffer cells), take up hæmoglobin particles coming from the disintegration of red blood corpuscles, which is going on in the body continually, remove the iron-free portion of the hæmoglobin, and form bilirubin. This in turn is carried by the blood stream to the liver, is taken up by the polygonal cells of this organ, is excreted into the bile capillaries, and through the bile ducts reaches the intestines. Here it is converted into urobilinogen by the bacteria of the intestinal tract; some is excreted in the fæces, and the remainder reabsorbed and carried to the liver by the portal vein, to be again taken up by the polygonal cells and excreted.

By the use of the method discovered by van den Bergh for the estimation of bilirubin in the blood it has been found that under normal conditions the blood contains a certain quantity of bilirubin—0.2 to 0.4 units—and that if from any disturbance in the body this increases to 4 units, the tissues of the body are stained yellow. Jaundice, therefore, develops as the result of an excess of bilirubin in the blood, or a bilirubinæmia. As suggested by McNee, bilirubinæmia may result from an obstruction of the bile ducts to the outflow of bile, as from a stone in the common duct; from damage to the polygonal cells of the liver interfering with the secretion of bile, as in toxic hepatitis from arsphenamine poisoning; or from increased destruction of red blood corpuscles, resulting in an excess formation of bilirubin, as in familial hæmolytic jaundice

In order to clearly understand how an obstruction to the outflow of bile, damage to the polygonal cells of the liver, or an excessive production of bilirubin may cause jaundice it is necessary to recall certain facts with reference to the structure of the liver and consider the pathological changes occurring under the conditions just mentioned. For this purpose McNee's conception of the structure of the liver lobule and the relationship to it of the portal vein, hepatic artery, and bile duct is very helpful. He represents the polygonal cells of the liver as a series of test tubes with the blind end towards the central vein and the lumen opening into the bile duct. On the outside of the tube, and between adjacent tubes, is a capillary network formed from the branches of the portal vein and the hepatic artery. This arrangement brings the blood in close contact with the polygonal cells of the liver. Under normal conditions the small quantity of bilirubin formed from the normal disintegration of red blood corpuscles is carried by the hepatic artery to the liver lobule, passes through the polygonal cells of the liver into the bile capillaries, and is excreted into the intestine. As has already been mentioned, part is reabsorbed as urobilinogen and the remainder excreted in the fæces.

If the common bile duct is obstructed the bile is dammed up in the bile capillaries and, as it cannot escape, is reabsorbed by the vascular capillaries and enters the central vein, thereby causing an excess of bilirubin in the general circulation, and a deposit of the pigment in the tissues of the body results. In jaundice due to obstruction of the outflow of bile the polygonal cells are normal and able to secrete bile, and the bilirubin formed by the reticulo-endothelial system is normal in quantity. If the polygonal cells of the liver become damaged from poisons carried to it by the portal vein or hepatic artery the secretion of bilirubin is interfered with. As a result, the quantity not secreted passes directly into the central vein, causing bilirubinæmia in proportion to the severity of the cell damage. Although the same poison may damage the red blood corpuscles and cause an increased formation of bile pigment, and even obstruc-

tion to the outflow of bile from pressure on the bile capillaries in the liver by the damaged polygonal cells, the primary and essential cause in this form of jaundice is damage to the polygonal cells themselves. In conditions causing an increased destruction of red blood corpuscles there is an excessive formation of bile pigment. The quantity of bilirubin formed and carried to the liver is too great for the polygonal cells to secrete rapidly enough. The excess, therefore, passes directly into the central vein, resulting in a bilirubinæmia In this form, known as hæmolytic jaundice, the polygonal cells are normal and there is no obstruction to the outflow of bile. All varieties of jaundice therefore result: (1) from interference with the outflow of bile; (2) from damage to the polygonal cells of the liver; (3) from increased destruction of the red blood corpuscles. Upon this theory of the development of jaundice McNee has suggested the following classification:

(1) obstructive hepatic jaundice;
(2) toxic or infective hepatic jaundice;
(3) hæmolytic jaundice

Experience has shown that all clinical cases of jaundice can be classified under one or more of these three varieties.

Our first object in the diagnosis of a case of jaundice should be to determine from the results of our clinical examination the primary cause of the jaundice; interference with the outflow of bile, damage to the polygonal cells of the liver, or increased destruction of the blood; and our second object, the consideration of the possible clinical causes of the variety or varieties of jaundice present. The clinical examination must include an accurate record of the patient's complaint, a complete physical examination, and an examination of the urine and fæces for bile and urobilin, and of the blood for signs of anæmia. In the history of the present illness it is important to secure as accurate an account as possible of the patient's symptoms at the onset of the jaundice and up to the time of observation, noting not only the sequence in their appearance, their duration and intensity, but the time relationship between their development and the first sign of jaundice. Careful inquiry should be made as to the colour of the urine and stools. A change in the colour of the urine may be noticed before the appearance of jaundice in the sclera and skin. The colour of the stools may provide the clue to the diagnosis. They may be clay-coloured from the onset of the jaundice, as in obstruction due to gall stones in the common duct; normal or darker in colour in hæmolytic jaundice; or normal in colour at the onset, later becoming temporarily lighter or clay-coloured, in toxic hepatic jaundice. This is the usual history in catarrhal jaundice which is a toxic hepatic form of jaundice.

The presence or absence of pain is of very great importance in diagnosis. Jaundice following attacks of colicky pain is nearly always due to an intrinsic obstruction in the common bile duct, usually a gall stone, less often a simple stricture, or carcinoma of the wall of the duct. In obstructive hepatic jaundice due to extrinsic causes, as from pressure from enlarged glands in secondary malignant disease, and in toxic hepatic or hæmolytic jaundice, colicky pain is usually absent, the patient complaining only of aching or soreness in the right upper quadrant of the abdomen. Other symptoms present at the onset may suggest primary disease of the liver, or disease of other organs with secondary changes in the liver or bile ducts, or disease of the blood-forming organs. A history of lassitude, loss of appetite and general weakness, with or without fever, followed later by nausea and vomiting is common with disturbances of liver function. While these symptoms occur in other conditions, their presence before, and persistence after, the appearance of jaundice is very suggestive of intrahepatic rather than extrahepatic disease as the cause of the jaundice, i.e., a toxic or infective hepatic type of jaundice. In the past history one

should especially enquire into the question of previous attacks of jaundice, recurring infections, upper gastrointestinal tract disturbances, and any illness suggesting disease of the liver or blood-forming organs, and should try to determine if the onset of the present attack of jaundice is or is not related to a former illness.

In the physical examination of the patient, special attention should be given to the examination of the liver and spleen for local signs of disease, and to other regions of the body for primary disturbances, as myocardial disease with failure, pregnancy, etc., that might affect the liver secondarily and cause jaundice In the examination of the liver its size, and the presence or absence of tenderness, are the two points of greatest value in diagnosis. The consistency and the presence or absence of irregularities are of lesser importance. Irregularities on the surface of the liver indicate intrahepatic disease as the cause of the jaundice, but unfortunately only the gross, and not the finer irregularities more commonly present, can be determined with any degree of certainty on physical examination. A definite enlargement or the presence of local or general tenderness of the liver points to intrahepatic disease as the cause of the jaundice. If one excludes cases of enlargement or tenderness due to venous engorgement from chronic myocardial disease with failure, to distension from bile in obstruction of the common duct, and to metastases from new growths, the finding of an easily palpable liver, more especially if associated with tenderness, indicates a toxic or infective hepatic type of jaundice. Metastatic new growths in the liver may cause a marked enlargement, but if jaundice is present it is more likely to be due to pressure on the common duct from metastases in glands than from secondary new growths within the liver. In certain cases of jaundice the liver may be smaller than normal. This is found in portal or atrophic cirrhosis, and in acute or subacute necrosis of the liver, commonly called acute yellow atrophy, a condition in which a toxic or infective hepatic type of jaundice is present. In the early stage the liver may be palpable; later it becomes smaller than normal, due to necrosis or atrophy. In acute cases of necrosis the size of the liver is of more importance in prognosis than diagnosis.

As the spleen is often enlarged in diseases of the liver and in hæmolytic types of jaundice, it is important to examine for a palpable spleen. The presence of a definite splenomegaly with little or no enlargement of the liver suggests that the primary cause of the jaundice is splenic or extrahepatic in origin. In the hæmolytic type of jaundice the spleen is usually palpable, seldom large; the liver is normal in size and not tender. In biliary cirrhosis both spleen and liver are markedly enlarged, tenderness is slight or absent, and the jaundice is permanent, becoming more severe as the condition progresses. In portal cirrhosis the spleen is just palpable, the liver moderately enlarged, normal or smaller than normal in size.

If the clinical history suggests disturbances of regions of the body other than the liver and spleen, which may secondarily affect the liver and cause jaundice, special attention must be given to the physical examination of the system or systems affected. In most cases valuable information can be obtained from the examination of the stools, urine and blood. A sample of the stool should be examined macroscopically and tested for bile pigment and the urine tested for bile pigment and urobilin. With complete obstruction of the common duct the urine contains bile, rarely urobilin; in toxic or infective hepatic jaundice, bile and urobilin; and in hæmolytic jaundice, urobilin and no bile. If a hæmolytic type of jaundice is suspected the fragility of the red blood corpuscles should be determined. The presence of a heightened fragility is diagnostic of familial or acquired hæmolytic jaundice. In recent years the van den Bergh test for

the detection of bilirubin in the blood has been employed in the differentiation of the various types of jaundice. This test gives a prompt "direct reaction" in obstructive hepatic jaundice, and an "indirect reaction" in hæmolytic jaundice, and is of use in the diagnosis between these two types. At the onset of toxic or infective hepatic jaundice a "biphasic reaction" is present, but later a "direct reaction" occurs in nearly all cases, which makes the test of little positive value in the diagnosis between an obstructive and toxic hepatic jaundice. The presence of a prompt direct reaction, therefore, is no indication for operative interference, unless the other clinical findings indicate that the jaundice is due to obstruction of the extrahepatic bile ducts.

With the data obtained from the clinical history and the physical and laboratory examinations, one proceeds to determine the variety of jaundice present. The diagnosis between a hæmolytic and an obstructive or toxic hepatic type of jaundice is not difficult. In the hæmolytic form the jaundice is rarely severe; the onset is usually insidious and the patient is not acutely ill, except in certain rare cases of acute hæmolytic anæmia. The liver is not enlarged and the spleen may or may not be palpable. The stools are normal or darker than normal in colour, and the urine shows urobilin and no bile. In the differential diagnosis between a primary obstructive hepatic type of jaundice and toxic or infective hepatic jaundice with signs of obstruction, correct diagnosis is often difficult. One must attempt to differentiate an obstructive intrahepatic lesion from one due to extrahepatic causes, for in the former operation is rarely indicated, while in the latter operative treatment is often necessary. The following points seem the most helpful in the differential diagnosis of these two types of jaundice: the presence of colicky pain indicates an obstruction of the common bile duct as the cause of the jaundice; if it is complete the stools are clay-coloured from the beginning of the jaundice, and the urine contains bile and usually no urobilin. An easily palpable liver, especially if associated with tenderness, suggests intrahepatic disease and a toxic or infective hepatic type of jaundice. The stools are usually normal in colour at the onset and later become paler or clay-coloured if signs of obstruction develop. The urine containe bile and urobilin.

Having decided upon the type of jaundice present, one must consider next the second object in diagnosis, the possible clinical cause. Bearing in mind the different causes of jaundice, their clinical manifestations, and the type of jaundice, according to the above classification, present in each, one can usually arrive at a correct diagnosis.

In this paper no effort has been made to consider in detail the different clinical causes of jaundice, as these are familiar to all, but rather to review our present knowledge of bile pigment metabolism and to indicate the way in which it can aid us in the clinical investigation of patients suffering from the symptom—jaundice.

The Origin of the Breath Sounds.

By D. A. MacFADYEN, B.Sc., M.A., 3T1.

I. Foreword.

Last winter the author was impressed with differences in the views of the origin of the breath sounds. A. G. McPhedran (1) stated that there are two distinct types of breath sounds, vesicular and tubular. The vesicular sounds are produced by vibrations of air in the alveoli and are produced independently; tubular breath sounds are produced by vibrations of air in the tracheobronchial tree. Contrary to this view was the opinion (approved by the department of medicine) of J. L. Uren

(2) in this journal. Uren wrote that the vesicular and tubular breath sounds have a common origin in the larynx.

Subsequent investigation of these opinions showed that the differences were significant for only one reason. For this reason this paper will review the outstanding contributions of various people and will conclude with a decision which is probably correct.

II. Contributions in Support of the Partition Theory.

The greater part of considerable pertinent experimental work was reviewed by G. E. Fahr (3), in 1927. This review will be presented in numbered summaries.

(1) Martini and Mueller investigated the source and transmission of bronchial breath sounds by recording graphically the free vibrations of the tracheo-bronchial system cut serially at different levels. They found:
   (a) With the mouth, nose, and tracheo-bronchial system intact that the frequency of vibrations was 400-600 per second.
   (b) When the system was cut below the larynx that the frequency of vibrations was 800 per second.
   (c) When the cut was made at the bifurcation of the trachea into the two main bronchi that the frequency was 1000-1100 per second.
   (d) When the cut was made at the bronchi of 5 mm. diameter that the frequency was 1200 per second.
   (e) When the cut was made at the bronchi of 4 mm. diameter that the frequency was 1300 per second.
   (f) When the cut was made at the bronchi of 3 mm. diameter that the frequency was 1700 per second.

They found also that bronchial breathing gives no overtones with a frequency as high as 1300 per second and that bronchial breath sounds have a frequency not less than 400 per second. They found that adult lung tissue gives sounds of frequencies 100-200 per second and that it transmits vibrations of only those frequencies.

(2) Schultze observed that, in tubes of 1 mm. diameter or less, friction renders bronchial sounds inaudible at the chest wall though some sound is conducted along the walls of the tubes and along the interstitial tissue.

(3) Bullar performed an ingenious experiment to determine the origin of the breath sounds. He sealed the left lung of a calf into a jar in which the pressure could be altered. The right lung was collapsed and outside the jar. One stethoscope was sealed into the jar and one placed on the right lung. When the pressure was lowered in the jar typical vesicular inspiratory sounds were heard from the left lung. These sounds were heard also when the main left bronchus was plugged. None were heard over the right lung with the passages open or closed. Since the two lungs and tracheo-bronchial tubes were in system Bullar concluded that the movements of air in the bronchi have no relation to the vesicular sounds and that the inspiratory vesicular sounds are caused by air entering the alveoli.

(4) Sahli heard normal vesicular sounds over a lung when the glottis was closed and pressure applied to the abdominal muscles. The lung protruded through a congenital sternal fissure.

(5) Fahr observed that after laryngectomy auscultation of the breath sounds from the seventh cervical to the third thoracic vertebrae revealed practically no change in the breath sounds.

Furthermore, Ignatowski and Von Lemeric (4) made observations from

an unusual case of spontaneous pneumothorax. They conclude that the expiratory vesicular breath sounds have their origin in the lung parenchyma and that they are not laryngobronchial sounds modified by transmission through the lung tissue They quote Sahli's observation in support of a parenchymal origin for the inspiratory vesicular breath sound and corroborate his work.

Emerson (5) gives clinical information pertinent to this problem. In Tuberculosis while the rales predominate the breath sounds are normal. Since rales are a late manifestation of Tuberculosis it is inferred that the breath sounds are first altered and then approach normal as the rales begin to dominate. The cause of rales is fluid in the terminal bronchial tubes; there would be no conduction of bronchial sounds. Therefore normal breath sounds, under conditions where bronchial sounds are not conducted, can only originate in the lung parenchyma.

III. Contributions Disputing the Partition Theory.

The most lively opponent of the hypothesis that the breath sounds originate independently was G. E. Bushnell (6). His experiments were subjective and, to the author's knowledge, were not corroborated by other investigators. Nevertheless, his results were received favorably by Norris and Landis (7). And nevertheless, considerable comment was published in different journals. A summary of Bushnell's work is presented.

(1) Bushnell practised opening the glottis wider than normally. With practice he was able to keep the glottis open during expiration. When the glottis was open widely sounds were not heard over the larynx and, concurrently, sounds were not heard over the chest despite precautions to ensure deep breathing.

With an open glottis the control of expiration was more difficult. To prevent an overfilling of the lung with air expirations were prolonged in lieu of forced expirations which were impossible. Still there were some "aspirate sounds' noticeable, and the fact that these were eliminated only occasionally was considered to be due to lack of practice in keeping the glottis open widely.

(2) How could the harsh and relatively high-pitched laryngeal sounds betransformed into the soft and low-pitched sounds heard over the lung? This was explained by a selective resonance by the thorax as a whole; high-pitched sounds are relatively inaudible because of the re-inforcement of the low-pitched sounds.

(3) He explained Sahli's lung observation in this way; the glottis being tightly closed the subject first raises the thorax and distends the abdomen by contraction of the diaphragm; this procedure causes a rapid to and fro motion of air between the glottis and the diaphragm and so creates a sound over the lung which resembles respiration and has the pitch of vesicular breathing. He considered this phenomenon due to an element which is sufficiently low in pitch to excite the thoracic resonance.

(4) He concludes with the opinion that the selective action of resonators (thorax and bronchial tubes) plays an important part in determining the characteristics of sound produced by movements of air in the respiratory system.

Bushnell's opinions were received unfavorably by Montgomery (8). Montgomery emphasized that the expiratory chest murmur was weaker in intensity, shorter in duration, and lower in pitch than the inspiratory chest murmur; he also emphasized that the expiratory laryngeal murmur was stronger in intensity, longer in duration, and higher in pitch than the inspiratory laryngeal murmur. As well, there are observations which are incon-

sistent with the hypothesis of the common laryngo-bronchial origin of the breath sounds. The first of these is that the voice sounds are heard with greater audibility on the right side whereas the inspiratory murmurs are heard with lesser audibility on the right side than on the left. In compensatory emphysema the inspiratory sound may closely approach the laryngeal sound in loudness, but there is no corresponding increase in the audibility of the voice sounds. Furthermore, many conditions, as in early and late pulmonary or pleural inflammation, or, as in hemiplegia, permit the normal transmission of the voice sounds when the breath sounds are diminished or absent. If it is assumed that the high-pitched and low-pitched sounds are both produced in the larynx, low-pitched whispers should be heard with greater intensity over the thorax than over the larynx because of the resonating power of the thorax. This assumption is inconsistent with the facts.

IV. Discussion of the Evidence.

The comments of Montgomery conclude a review of the observations and opinions of the outstanding contributors to this problem. A summary of the evidence so far accumulated shows:

(1) that Bushnell's experience should be approved cautiously since it is subjective. It has not been corroberated.

(2) that it is difficult to reconcile Bushnell's explanations with the findings of Bullar, Martini and Mueller, and Schultze, and, with the inferences of Montgomery. Bullar's demonstration that movements of air in the bronchial tree have no influence on the vesicular murmurs and Martini's observations that the frequency of vibrations of the vesicular sounds is from 100-200 per second, whereas bronchial sounds have a frequency not less than 400 per second, indicate, at least, that the alveoli are capable of typical vesicular breath sounds. Furthermore, the likelihood of reinforcement of sounds originating in the upper respiratory tract by the alveoli is very slim when judged from these results and from Schultze's observation that in tubes of 1 mm. diameter friction renders bronchial sounds inaudible at the chest wall.

(3) that Bushnell's view of the respiratory system as a series of resonators explains the observations of Sahli, of Fahr, and of Ignatowski and Von Lemeric.

From the evidence accumulated the author believes that the vesicular sounds have their origin in the parenchyma of the lung. They are distinct in origin and quality from the tubular breath sounds which are produced in the respiratory tract in its upper part and in its part intermediate down to the bronchi of 4 mm. diameter.

V. The Relation of Breath Sounds in Disease to This Problem.

What is the practical significance of these differences of opinion? A paper by Montgomery and Eckhardt (9), was used as a basis to decide this important question.

The character of the sound heard over the chest depends on the effect of the tissues on the acoustic properties, interference, absorption, resonance, reflection, and diffusion. Diffusion is considered the most important property, though resonance and reflection can become as important. Special diffusion occurs when the lung is displaced or replaced by large quantities of homogeneous medium such as fluid: a homogeneous medium conducts sound equally well in all directions. Special reflection occurs at the interfaces of altered density such as the interface between fluid and tissue.

In the normal chest there is no diffusion, but there is special reflection at the interface between the lung and chest wall. This reflection diminishes the audibility of the vesicular sounds, but it does not indicate the source of the vesicular sounds.

When the lung is solid there are no audible vesicular sounds, though special diffusion and special reflection are absent. Vesicular sounds cannot originate from the parenchyma since the alveoli do not bear air. Assuming a laryngeal origin for the vesicular sounds their absence in this condition may be explained by the selective resonance of the thorax; a solid body vibrates at higher frequencies than air-bearing bodies and thus it will resonate vibrations of higher frequency and so bronchial breathing will be heard. The difference between the two hypotheses is that bronchial breathing heard over the chest indicates, on one hand, an extended conduction of sound, and, on the other hand, an altered selection of sound.

When the lung is solid but separated from the chest wall by fluid, there are no vesicular sounds heard over the chest. Special diffusion of sound between the lung and chest wall lessens the audibility of sounds conducted through the lung. A parenchymal origin or a laryngo-bronchial origin suffices equally well for an explanation of the absence of vesicular sounds and for the likely absence of bronchial sounds.

When the lung is air-bearing, but relaxed and separated from the chest wall by fluid there are no sounds over the chest. There is special reflection at the interface between the relaxed lung and the fluid as well as special diffusion through the fluid. It is more likely that sounds of both types will be absent in this condition than it is in those conditions. The explanation of this absence of breath sounds is the same as it was for those.

When air, liquid, or solid is present in abnormal proportions an explanation for these findings is afforded satisfactorily by both hypotheses. Nevertheless, a critical experiment or observation is necessary: for the problem is concerned with the interpretation of sounds heard over the chest. Are these sounds to be interpreted as pneumonia produced in the lung or outside the lung? If laryngeal or tracheo-bronchial disorders can be manifested by changes in the breath sounds heard over the lung then the interpretation of these sounds is limited and confusing.

VI. The Effect of Phrenicotomy on the Breath Sounds.

Keith (10), emphasized that the most important part of the lung is that near the base and that immediately under the pleura. Since the function of the basal lung depends on the movements of the diaphragm and since the greatest distension of the alveoli is in the direction from the root to the costophrenic angle it was thought of critical importance to investigate the breath sounds before and after Phrenicotomy. Phrenicotomy was performed in March, 1929, and the examinations for these records were made in August, 1929, at the Manitoba Sanatorium, Ninette.

Each of the three patients examined had tuberculosis, and so the observations are subject to some modification. These patients were chosen from a group of twenty-two because examination showed:

(1) that the disease was limited to the apices
(2) that in every case the diaphragm was completely immobilized.
(3) that every patient chosen was a male.

Physical and fluoroscopic examinations were made by at least two internes, working independently.

In all, the side affected gave altered breath sounds. The alteration was estimated by using as controls the sounds heard over the unaffected side and the sounds recorded from the affected side before operation. In all, the alteration was the same; the apices of both lungs gave the same characteristic broncho-vesicular sounds; the rest of the unaffected lung gave normal vesicular sounds; the rest of the affected side gave diminished vesicular sounds in that part near the apex and gave no sounds, whatever, over that part extending the breadth of one intercostal

space above the level of the immobilized diaphragm.

These observations indicate that where distension and relaxation of the alveoli is impaired the breath sounds are impaired. It is unlikely that the collapse of a small portion of lung tissue would impair, to a noticeable degree, the resonating power of the thorax. It is more likely that the collapse of lung tissue would favor the transmission of tracheo-bronchial sounds since compact tissue will resonate sounds of higher pitch than will lung tissue in the more porous normal condition.

VII. Conclusions.

It is believed that the origin of the breath sounds is graced, legitimately, with theory. It is believed, too, that the evidence may be summed to substantiate the partition theory of the breath sounds, that is,—the theory that the vesicular and tubular breath sounds are mutually independent in origin.

(1) McPhedran, A. G., Lectures in Medicine, 1928-1929.

(2) Uren, J. L., U. of T. Medical Journal, Vol. IV., No. 3, p. 90, 1927.

(3) Fahr, G. E., "The Normal Chest," by J. A. Myers, 1927.

(4) Ignatowski, A. J., and Von Lemeric, M., Amer. Rev. Tuberc. Abstracts, Vol. XVI., No. 3, p. 49.

(5) Emerson, "Clinical Laboratory Diagnosis," p. 270.

(6) Bushnell, G. E., J.A.M.A., Vol. LXXVII., p. 2104, 1921.

(7) Norris and Landis. "Diseases of the Chest and the Principles of Physical Diagnosis," p. 68, 1924.

(8) Montgomery, C. M., Amer. Rev. Tuberc., Vol. XVIII., No. 2, p. 205, 1928.

(9) Montgomery and Eckhardt, "Pulmonary Acoustic Phenomena," 10th report, Henry Phipps Institute, Phila., 1915.

(10) Meakins and Davies, "Respiratory Function in Disease," p. 18, 1925.

Insulin and Surgery.*

By J. C. THOMAS, 3T1.

The effect of the discovery of insulin on surgery is best shown by a study of the surgical diabetic. The surgical diabetic is the most serious diabetic, the diabetic who dies. Joslin has found that from 1923 to 1926 the diabetic mortality for surgical cases at the Diaconess Hospital was 11.5%; the medical mortality during the same period was 1.7%.

A comparative study of the mortality rate among diabetics before and after the discovery of inslin shows a reduction in the number of deaths from 29.5% in 852 cases to 14% in 1,389 cases. These are averages of the reports of 12 authors whose reports include all types of operations. The mortality as given by these authors varies widely, due to the reference of some to mild or moderate cases and of others to more severe cases. (Table 1.)

Reed (1) in a report of the mortality among such cases finds the average to be 34% before and 12.07% since insulin. These figures show a greater reduction in the number of deaths than the above do. However, it should be pointed out that the pre-insulin figures used to determine this higher average include

* A paper presented before the Alpha Omega Alpha Fraternity, November 25, 1929.

TABLE I.

Before Insulin.

Authors.	Number of cases.	Mortality.
Young (11)	99	16.7
Krecke (41)	20	30
Karewski (42)	137	33
Berkman (18)	159	9.5
Joslin (8)	27	18
Stetten (13)	17	29
Weeden (3)	160	36.8
Strouse (17)	38	31
Mason (2)	41	22
Menninger (9)	47	42.5
Fischer (15)	86	48.5
Rabinowitch (10) .	21	38.1
	852	29.5 (Average)

After Insulin.

Authors.	Number of cases.	Mortality.
Reed (1)	64	19
Mason (2)	60	15
Allen Sherrill (20)	14	35
Weeden (3)	12	16.6
John (4)	35	20
Foster (5)	103	12
Judd (6)	664	3
Bauman (7)	17	12
Joslin (8)	322	11.5
Menninger (9)	22	14.5
Rabinowitch (10) .	76	5.2
	1,389	14 (Average)

many more reports based on a series of cases of diabetic gangrene and infections alone. Such cases, as we shall see later, have a higher mortality, therefore the comparison can hardly be considered as giving a true picture of the effect of insulin on diabetic surgery.

What are the operations upon diabetics? According to Joslin (8), amputations of an extremity or part of an extremity, together with superficial and deep septic processes such as abscesses, ulcers, and carbuncles, constitute nearly one-half of the total operations. The mortality for this half of diabetic surgery accounts for more than two-thirds of the surgical mortality. In a series of cases Joslin (8) and Reed (1) have classified surgical operations upon diabetics into two main groups. The first group includes amputations and infections, and is called the preventable group. The mortality for this group is much higher than for the second group which includes appendectomies, thyroidectomies, laparotomies, etc., under the head of general surgery. In this group the mortality rate since the discovery of insulin compares very favorably with that of similar cases in non-diabetics.

TABLE II.

Joslin, 1923-1926.

Operations	Total	Fatal	Mortality
Amputations .	89	17	15.6%
Infections	56	6	
General surgery	177	14	7.9%

Reid, 1923-1928.

Operations	Total	Fatal	Mortality
Amputations .	28	9	25.5%
Infections	15	2	
General surgery	21	1	4.7%

Let us consider the same fact from another angle. The following figures (Table III., compiled by Rabinowitch (10) at the Montreal General Hospital show that, although the death rate from diabetes in a series of hospital-treated cases has decreased, not only has the incidence of gangrene not decreased but it has accounted for a very large percentage of the total mortality from diabetes.

TABLE III.

Year	No. of Cases	Gangrene	Deaths All Cases	Deaths from Gangrene
1921-22	208	6 or 2.8%	25 or 12 %	4 or 16 %
1923-24-25	600	28 or 4.6%	23 or 3.8%	9 or 39.1%

Obviously then gangrene is one of the most important complications of diabetes and certainly the most important of all surgical conditions in diabetes.

What effect has insulin had on diabetic gangrene?

TABLE IV.

GANGRENE AND INFECTIONS

Before Insulin.

Author.	Mortality.
Pilcher (22)	50 %
Bruce (23)	50 %
Gardner (26)—	80 %
Fischer (15)	72.7 %
Fitz (24)	50 %
Mason (2)	35 %
Blotzner and Fitz (19)	30 %
Binney (21)	60 %
Joslin (8)	60 %
Stetten (13)	60 %
Average	51.7 %

After Insulin.

Joslin (8)	14 %
Blotzner and Fitz (19)	15 %
Mason (2)	19 %
Reed (1)	25.5 %
Eliason and Wright (25)	41.5 %
Average	23.5 %

A comparison of the mortality before and after insulin shows a reduction in the number of deaths in cases of diabetic gangrene and infections treated surgically from an average of 51.7% to 23.5%. Insulin is saving the lives of diabetics suffering from gangrene and septic processes.

Has insulin made it possible to save limbs from amputation when affected with gangrene? This question cannot be answered quantitatively either positively or negatively. While it is beyond the scope of this paper to discuss the pathology of diabetic gangrene, brief reference must be made to it here. Gangrene in the diabetic is taken as presumptive evidence of arteriosclerosis. Joslin (8) has shown by a study of autopsies upon diabetic patients that 70% of those whose disease had lasted less than five years showed arteriosclerosis. All the others with a duration of more than 5 years had sclerotic arteries. Evidence was also obtained by X-ray examination. The percentage of total diabetics examined (324) showed arteriosclerosis for successive five-year periods of duration of the disease as follows:

The first five years	40%
The second five years	56%
The third five years	83%
From the fourth five years on	92%

In a statistical study Joslin (8) points out that the average age of diabetics at death from 1894 to 1914 was 44.8 years with the average duration of diabetes of 4.7 years. From August, 1922, to July, 1926, after insulin was in use, the average age was 54.2 years, with the average duration of the disease of 7.7 years. In this era the incidence of diabetic gangrene rose to 47%, from 15% in the former. Thus insulin treatment by prolonging the life of the diabetic has brought him into the arteriosclerotic period in life when he is more liable to arteriosclerosis and consequent gangrene. Therefore we can scarcely expect to find the use of insulin in the treatment of diabetic gangrene an effective therapeutic agent. The efficacy of insulin and dietetic treatment in the healing of diabetic gangrene must be wholly dependent upon the degree of arteriosclerosis present and the impairment of circulation resulting from it in the affected part.

In 1913 Stetten (13) published a series of cases of diabetic gangrene treated conservatively with splendid results. In 17 cases there were only 5 deaths. The average duration of the treatment was 2¾ months. In 8 cases a cure was effected by incision of the infected area or by amputation of a toe only. His cases were very carefully treated following three main principles. (a) There was systemic treatment of the diabetes and prophylaxis against the development of dangerous compli-

cations, especially coma. This was accomplished by diet. (b) An attempt was made to improve the circulation in the extremities by hot baths and dry hot air. (c) The local infection was treated by rest and asepsis using dressings of sterile salt solution to avoid strong antiseptics.

Since the discovery of insulin there have been reported cases where gangrene has healed under insulin treatment without surgical interference.

Dupré (22) reports such a case of a gangrenous toe and foot in a man, age 75, which cleared up in 3 months so that the patient could walk on the foot again and feel no discomfort beyond stiffness in the knee from prolonged disuse.

Mason (2) in 1925 quotes the following from Wilder: "With insulin one can be more conservative in amputations." From his own experience Mason says he has never seen a gangrenous toe with or without insulin heal spontaneously and completely. In most of the cases where a conservative amputation has been attempted a second one higher up has been imperative at a later date.

Again in 1928 Mason (28) reports a series (from 1926 to 1928) of 24 cases of diabetes with gangrene. Two died within a few hours of admission. Fourteen had extensive gangrene of one foot. Five of these, or 36%, obtained complete cure by medical means alone. Eight had cangrene confined to one or more toes. Five of these or 63% recovered completely without surgical interference.

Blotzner and Fitz (19) studied a series of cases of diabetes with gangrene. In going over their material they were not particularly struck by the effect of insulin upon the healing of gangrene once it has developed. Except for a few cases of superficial gangrene, there have been few cases which have healed spontaneously under medical care alone.

Gray (29) reports a case with moist gangrene of the foot which completely healed in four months with medical treatment to control the diabetes using insulin. This patient recovered sufficiently well to do her own housework.

This review of the experience of various men suggests a more hopeful future in the treatment of diabetic gangrene using insulin. Statistics cannot be derived from so few cases and until more have been recorded we can only conclude that insulin per se will not save limbs from diabetic gangrene but by its use diabetes can be rigidly controlled, making possible more conservative surgical treatment of the gangrenous part.

Insulin in Non-Diabetic Surgery.

Almost immediately upon the discovery of insulin and its value in the treatment of diabetes attempts were made to use it in non-diabetic conditions. During the past 6 years a fairly extensive literature has grown up on the use of insulin in the treatment of various post-operative conditions and, if the extent of the literature is any indication, the use of insulin must be very widespread in surgical clinics today.

There appeared in 1923 the pioneer work of Thalhimer (30). He reported successful treatment of 3 cases of post-operative acidosis with glucose and insulin, noting an almost immediate cessation of vomiting and ketosis. He noted that this treatment was successful after the injection of glucose alone had failed. Thalhimer based his treatment on the fact that insulin when injected subcutaneously causes an increase in the rapidity of the utilization of glucose in the body, both normal and diabetic.

This type of treatment was elaborated by Fisher (31) and his coworkers. They used insulin with glucose injections in the pre-operative and post-operative treatment of acidosis. The authors believe that the introduction of insulin supplies an unknown factor in non-diabetic acidosis to make immediately available for body needs the introduced carbohydrate. Since time is always an important factor in non-

diabetic acidosis the tremendous advantage of insulin and glucose over glucose alone can be readily appreciated. One case which remained practically unchanged at the end of 24 hours by the use of glucose alone by rectum showed an immediate disappearance of ketosis on subsequent injection of insulin.

In a more recent paper Fisher (32) reports further success with this treatment of post-operative shock and non-diabetic acidosis. In this paper the author discusses fully the rationale behind this treatment.

Ginsberg (33) reports an interesting and carefully studied case of traumatic shock which he successfully treated with glucose and insulin. He records the CO_2 combining power of the blood which rose from 37 volumes per cent. before treatment to 58 per cent after.

Dolan (34) reports a series of cases of non-diabetics in which post-operative vomiting was controlled by giving glucose and insulin before and after operation. The author stresses its value in the cases where vomiting is established and as a prophylactic measur in not too robust patients where lesser degrees of vomiting are both distressing and dangerous.

Wade (35) in a series of 40 cases, including 18 with traumatic shock and 12 cases of post-operation shock found this treatment more satisfactory than saline or glucose injections alone.

Padgett and Orr (36) recently undertook an experimental test of the value of glucose and insulin in the treatment of traumatic shock. Dogs were anaesthetized with ether and shock was produced by hammering the thigh muscles of one leg, followed by occasional massage until the blood pressure fell below 70 mm. with a definite tendency to continue falling. Control animals were used and the value of glucose alone as well as glucose and insulin was tested.

In no instance was any evidence noted that the addition of insulin in any way caused any specific aid that could be determined by change in blood pressure or general condition of the animal. Glucose alone acted as favourably as the glucose-insulin combination. The authors conclude that from the experimental standpoint the glucose and insulin seem to be no more beneficial than treatment with hypertonic solution of glucose or sodium chloride.

Andrews and Reuterskiole (37) studied the action of insulin in a number of patients suffering from post-operative acidosis. The blood sugar was closely followed every 15 to 30 minutes. From a series of carefully controlled experiments the authors conclude that the use of insulin and glucose in patients, who are suffering from post-operative conditions and are therefore unavoidably dehydrated, is a highly dangerous and useless procedure. In post-operative acidosis glucose and water are needed.

In a study of carbohydrate metabolism in hepatic disease Ravdin (38) has found that the administration of dextrose previous to the operation improves the condition of the patient and reduces the operative risk. He points out that under insulin influence no more glycogen is deposited in the liver of the normal animal than is deposited in control animals receiving a similar amount of glucose. In fact it may even retard the glycogen deposition.

As yet no evperimental evidence has been presented to show how glycogen deposition may be affected in the severely injured liver by insulin. Until such evidence is presented insulin should be used cautiously and if at all, only after dextrose has been administered.

However, there is a small group of patients suffering from severe hepatic injury in association with an apparent diabetes. In these the fasting blood sugar is high and here insulin should be given with glucose.

Since chloroform and ether both give rise to a hyperglycemia after which a reduction of liver glycogen can be demonstrated, the author believes that whenever an inhalation anaesthetic is used dextrose should be

given before, and during or immediately after the operation.

McLean (39) has studied the effect of glucose, insulin and Na H CO_3 injection in non-diabetic ketosis. Ketosis with acetonuria was produced by 40-hour starvation. Fifty grams of glucose caused ketosis to disappear in one hour. Twenty grams of $NaHCO_3$ were given, but the ketosis still remained after 8 hours. Fifty grams of glucose and twenty units of insulin had no effect whatever on the acidosis. There was hypoglycemia and yet it did not result in any decrease of the time during which the acidosis persisted.

Joslin (8) states that it is remarkable that the tissues of non-diabetic animals narcotized with ether produce for less insulin than normal or even diabetic animals do. Best, Smith and Scott (40) have noted that there is less insulin in the blood of rabbits under ether anaesthesia.

Therefore, though the patient has presumably a quantity of insulin in his tissues, yet its production may be temporarily in abeyance due to the anaesthetic, and he may be tided over this period by the injection of insulin.

The use of insulin in the non-diabetic surgical case is still a debatable point. At present there is no definite scientific evidence that the use of insulin is necessary or beneficial. If, however, after giving glucose the acidosis persists, the use of insulin seems to be justified by the series of successfully treated cases.

Summary.

1. The death rate in the surgical diabetic since insulin has been reduced to less than one-half.

2. Necessary surgical operations in unrelated conditions such as appendicitis, cholecystitis, etc., in diabetic cases properly controlled by diet and insulin do not raise the mortality rate.

3. The mortality among diabetics suffering from gangrene has been reduced by the use of insulin in addition to diet Surgical interference has become more conservative because of the use of insulin. Thus many lives have been saved.

4. Insulin and glucose have been used successfully in the treatment of post-operative acidosis in non-diabetic patients. Its use here has been challenged and its value is still debatable.

Bibliography.

1. Reed, J. A. Surgery, Gynec. and Obst. 1928, 48, p. 44.
2. Maon, E. H. Canadian Med. Asso. Journal. 1925, 15, 601.
3. Weeden, M. W. J.A.M.A. 1924, 82, 1165.
4. Johns. Arch. Int. Med. 1927, 39, 67.
5. Foster, N. B. J.A.M.A. 1925, 84, 572.
6. Judd et all. J.A.M.A. 1926, 86, 1207.
7. Bauman. Surg. Gynec. and Obst. 1925, 41, 272.
8. Joslin. Treatment of Diabetes Melletus. 4th Ed. 1928.
9. Menninger. Surg, Gynec and Obst. 1925, 41, 454.
10. Rabinowitch. Canadian Med. Assoc. Jour. 1927, 17, 27.
11. Young. Bost. Med. and Surg. Jour. 1923, 188, 767.
12. Berkman. Minnesota Med. 1921, 4.
13. Stetten. J.A.M.A. 1913, 40, 1126.
14. Morrison. Bost. Med. and Surg. Journ. 1916, 175.
15. Fischer, H. (Abst.). J.A.M.A. 1915, 64, 282.
16 Jones. Bost. Med. and Surg. Journ. 1923, 185, 483.
17. Strouse. Quoted by Menninger (9) Surg. Clin. (Chicago). 1916, 2, 37.
18. Berkman. Lancet. 1916, 36, 309.
19. Allen and Sherrill. Journ. of Met. Research. 1922, 2, 966.
21. Binney. Quoted by Joslin (8).
22. Pilcher. Long Island M.J. 1910 iv., 57.
23. Bruce. Can. J.M. and S. 1914, 36, 12.
24. Fitz. J.A.M.A. 1919, 60, 2610.

25. Eliason & Wright. Surg. Gynec. & Obsts. 1927, 44, 253-2100.
26. Gardner. Rhode Is. M.J. 1922, V. 177.
27. Dupré. Br. Med. J. 1924, ii., 12.
28. Mason. Can. Med. A. J. 1928, 19, 76.
29. Gray. J. Lab. and Clin. Med. 1927, xii., 472.
30. Thalhimer. J.A.M.A. 1923, 81, 383.
31. Fisher & Snell. J.A.M.A. 1924, 82, 699.
32. Fisher. Surg. Gyn. & Obs. 1926, 43, 224.
33. Ginsberg. J.A.M.A. 1924, 82, 1517.
34. Dolan. Can. Med. Assoc. J. 1927, 17, 431
35. Wade. J.A.M.A. 1928, 90, 1859.
36. Padgett & Orr. Surg. Gynec. & Obs. 1928, 46, 783.
37. Andrews and Reuterskiold. Surg. Gynec. & Obs. 1928, 47, 665.
38. Ravdin. J.A.M.A. 1929, 93, 1193. (Oct. 19).
39. McLean. Proc. Ry. Soc. Med. 1927, 20, 309.
40. Best, Smith & Scott. Am. Jour. Phys. 1924, 68, 161.
41. Krecke. Quoted by Menninger (9).
42. Karewski. Quoted by Menninger. (9).

Dyspnoea.*

By C. B. WELD, M.A., M.D. (2T9).

Before discussing Dyspnoea, a few words in brief review of the physiological control of normal respiration are in order.

Control of Respiration.

(a) Chemical.
  (1) Acidity of the respiratory center and carbon dioxide tension of the center.
  (2) Oxygen tension of the center.

(b) Nervous control.

(a) Chemical Control.

The acidity of the respiratory center (as represented by the symbols "CH" or "PH") is perhaps the most important factor. In normal people, it alone is responsible for the volume of pulmonary ventilation. We all know that acids are constantly being produced by the body in the course of its normal processes, that these acids are first neutralized or buffered by the blood, and that to compensate, the excretory organs then dispose of more acid than basic substances. We have not sufficient space to develope this subject, involving as it would a discussion of the system of blood buffers, the nine Van Slyke areas, and the detailed function of lungs and kidneys. Suffice it to say that in order to maintain the normal acid—base equilibrium, the acids must be excreted as rapidly as they are produced, and the blowing off of carbon dioxide through the lungs is one of the most sensitive and flexible methods of excreting these acids.

In ordinary life, where the carbon dioxide combining power is fairly constant, the metabolic acids are closely reflected by the carbon dioxide tension of the blood. These together act upon the center in such a way that the CO_2 expired parallels the CO_2 production. In other words, the respiratory volume parallels the CO_2 production, and this varies with the metabolic rate.

J. H. Means ("Medicine," 1924) has calculated that in a normal average man, 3.67 litres of air per minute must be breathed in order to keep the carbon dioxide alveolar tension down to the proper figure, while only 3.00 litres would have to be breathed in order to maintain proper oxygen saturation of

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the blood. He suggests that the carbon dioxide control of respiration may act as a safeguard from asphyxia, as it always maintains an excess of oxygen in the alveoli.

The oxygen tension of inspired air in normal life and variations in oxygen saturation of the blood have no effect on respiration. However, a marked oxygen lack can stimulate the respiratory center, as is evidenced by the well-known "Forced Breathing" experiment. In this physiological demonstration, breathing (often of a periodic type) commences again after a period of apnoea before the carbon dioxide tension of the blood has regained its normal level. Means states that periodic breathing and cyanosis are pathognomonic signs of anoxemia.

(b) Nervous Control.

While the actual volume of pulmonary ventilation is controlled by chemical means, it is obvious that the nervous mechanism plays an important part in ordinary respiratory control. One can voluntarily alter one's breathing rhythm and volume. Respiratory acts cease during swallowing. Ventilation increases markedly at the very start of exercise before demonstrable chemical changes have occurred. In certain nervous upsets such as hysterical states, respiration may be greatly altered.

These examples show that nervous control is an important factor in making our respiratory cycle the easy unconscious process that it is in normal life. As Means says, it prevents "Respiratory Ataxia," acting as a governor and preventing wide fluctuations of a periodic type which would occur if chemical control existed alone.

Dyspnoea.

Means (Medicine, 1924), has given the following definition which Meakins (C.A.M.J., Jan., 1925), has adopted.

"Dyspnoea is the consciousness for the necessity for increased respiratory effort." "It will occur whenever the respiratory mechanism cannot with ease functionate to the extent that bodily processes require."

The call for respiration may come from any tissue, but the perception of the call is referred only to pulmonary functions. The word describing an objective increase in respiration is hyperpnoea, and it is important that we should recognize the difference between hyperpnoea and dyspnoea. Even a normay person may by work cause a hyperpnoea great enough to be distressing, which is dyspnoea. The degree of hyperpnoea necessary to cause dyspnoea varies greatly with the individual, which is understandable if one tries to explain why the respiratory act can become conscious.

Suppose the full vital capacity of the lungs were to be utilized in each respiration. This would entail a considerable degree of unaccustomed physical effort which would certainly become perceptible to the consciousness. Thus it is obvious that one's vital capacity is largely responsible for determining the degree of hyperpnoea necessary to cause dyspnoea. Athletes have a greater vital capacity than normals and consequently can do more physical work than normals before the increased respiratory effort becomes distressing Should the hyperpnoea be manifest in a more rapid breathing than in increased depth of breathing, this increased rate will soon become tiring and the effort will become conscious.

Hence the statement that anything increasing the demand for pulmonary ventilation, and anything decreasing the possibility of pulmonary ventilation, tends to cause dyspnoea. In more detail, some of these causes are discussed below.

I. Causes Increasing the Demand.

(A) Increased Metabolic Rate.

In any one individual the gaseous exchange will vary directly with the metabolic rate.

(1) Work. Physical exercise is the most potent cause of an increased metabolic rate and of increased demand for pulmonary ventilation. Moderate-

ly heavy work will increase the metabolic rate fourfold, so it is obvious that if there is any impairment to lung ventilation, a small amount of work will cause dyspnoea, or respiratory distress.

(2) Hyperthyroidism may be associated with a basal metabolic rate of 150 or 200% of the normal. This means that even when at rest there must be nearly double the usual amount of work done by the lungs, so that if they are at all diseased dyspnoea is rendered more likely. Of course in this state bodily efficiency during exercise is impaired, and there is apt to be heart damage, both of which are added causes of dyspnoea.

(3) Other causes of increased metabolic rate are less active and so less likely to result in dyspnoea. For example, there is an increase in Basal metabolic rate of 7.2% per degree Farenheit rise in temperature. Even at 105 degrees the B.M.R. would be only 147%.

After a heavy meal the metabolic rate may rise as high as 120%. These can be but minor causes of dyspnoea, and always associated with others.

(B) Disturbed Acid—Base Balance of the Blood.

It is true that factors increasing the metabolic rate, also increase the production of carbon dioxide, and so increase the breathing by changing the acid-base balance. This is a normal physiological mechanism, however, and the causes referred to in this heading are those more permanent changes in the alkali reserve such as occur in the acidoses of

(1) Diabetes.
(2) Renal insufficiency.
(3) Carbon dioxide acidosis.

It is well to realize that if the alkali reserve is low, an increased degree of pulmonary ventilation will be necessary in order to excrete a given amount of carbon dioxide through the lungs. At first thought this might not be apparent, because if the alkali reserve is low and the PH at all constant, then the carbon dioxide tension of the blood must be low.

However, if the carbon dioxide tension is low there will be less diffusion through the lungs and CO_2 will pile up in the blood, promptly raising the acidity and stimulating the respiratory center.

Hence in these acidoses there is call for increased respiratory effort, there is also a diminished ability of the blood to carry carbon dioxide, and therefore heart or lung function will be more easily strained and dyspnoea result.

(C) Diminished Ability of the Blood to Act as Carrier for the Respiratory Gases.

Obviously, if the circulation fails to transport the oxygen and carbon dioxide as freely as it usually does, then oxygen will be lacking or carbon dioxide will be high. Either cause (the anoxemia of the center or the acidosis) will stimulate the respiratory center, increase the respiratory effort, and render dyspnoea more likely.

(1) The blood itself may be at fault, as in anemia, and carbon monoxide poisoning, where the oxygen-carrying capacity is chiefly at fault.

Cases of acidosis, as already discussed, may cause dyspnoea, primarily because of a deficient CO_2 carrying capacity.

(2) There may be circulatory impairment, even though the blood itself may be normal, such as in cases of myocardial failure. This, of course, results both in diminished oxygen intake and diminished carbon dioxide output, and if the failure is severe, the dyspnoea may be very distressing. Sudden attacks of auricular fibrillation would give such a dyspnoea. In the more chronic lesions, secondary effects, such as chronic passive congestion of the lungs, are more likely to be the cause of the dyspnoea.

(D) Nervous Causes.

The actual control of the respiratory act is through the chief respiratory center, situated in the medulla. This

center is stimulated by the respiratory hormones already discussed, and it also receives nervous stimuli from other parts of the brain and body. For example, stimulation of the skin as by cold water or by certain actinic rays, will cause increased breathing. Stimulation of the mucous membranes of the nose and throat by pungent gases, or of the glossopharyngeal nerve as in swallowing, temporarily inhibits breathing and must hence be followed by increased breathing. Hysterical states, too, may cause hyperpnoea, and many patients become so frightened when they realize that breathing is difficult, that the hyperpnoea is accentuated.

These cannot be causes of very great hyperpnoea, but if pulmonary reserve is much lessened they may certainly cause dyspnoea

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II. Causes Decreasing the Possibility of Adequate Pulmonary Ventilation.

(A) Lessened Vital Capacity.

The role of vital capacity in determining the pulmonary reserve and hence in determining the degree of hyperpnoea possible before dyspnoea results, has already been pointed out. The vital capacity may be very greatly lowered, and many disease processes which can cause dyspnoea do so chiefly by diminishing the vital capacity. It ranks with the increased metabolic rate due to work in first importance as a common cause of dyspnoea

Some of the more important causes of a lessened vital capacity are: Pneumonia, Acute Pulmonary Edema, Bronchiolitis, Pneumothorax, Pleural Effusion, Fibrosed Pleura, Fibrosed Lung, Pulmonary Emphysema, Chronic Passive Congestion of Lung, Pulmonary Tuberculosis, Hyperthyroidism, and Thoracic Tumors, especially those about the Hylum.

All of these examples so lower the pulmonary reserve that a comparatively slight increase in demand for pulmonary ventilation might easily result in Dyspnoea.

In the chronic conditions such as pulmonary there may be a compensatory increase in the carbon dioxide combining power of the blood, reducing somewhat the amount of respiration necessary. However, this results in a tendency to anoxemia, and the dyspnoea when it does appear is liable to be very distressing. In the acute conditions, of course, there is no chance for any such compensatory mechanism to act, and respiratory distress is more easily elicited.

(B) Obstruction of Air Inlet.

This group of causes is very similar to the last group, and possibly do not deserve a separate heading. However, foreign bodies in the trachea, edema of the glottis, allergic reactions such as asthma, and mediastinal tumors, are all examples which partially prevent the in and out flow of air.

During easy, slow respirations such as would occur with the patient at rest, the vital capacity may be but little affected; while if muscular exercise is indulged in and forced breathing required, maximum filling of the lungs would be made more difficult and dyspnoea result.

(C) Interference with the Gaseous Interchange Between the Aveoli and the Blood

As the whole purpose of the respiratory act is to bring the proper kind of air into contact with the respiratory epithelium, altered functioning ability of this epithelium is vastly important. It is believed by most physiologists that the passage of gases through the aerating surfaces is purely a physical phenomenon. Consequently, then, in such a condition as pulmonary emphysema, where the area of aerating epithelium is reduced, the total diffusion rate is decreased. In pneumonia, too, the alveoli are filled with exudate and the area of aerating epithelium decreased. In pulmonary edema the presence of a foam in the lung parenchyma may greatly impede the diffusion of gases. A swelling or edema of

the respiratory epithelium such as occurs in poisoning with irritating gases, in allergic reactions, and in inflammatory processes may also act in the same way. In this connection it is well to remember that carbon dioxide diffuses some twenty times as fast as oxygen, which suggests that anoxemia rather than increase in acidity, is the cause of the hyperpnoea.

(D) Painful Lesions of the Thorax.

It is obvious that such conditions as lacerations, fractured ribs, or pleurisy, which cause pain on movement of the thorax, will make one aware of one's breathing. They may readily prevent normal chest expansion from occurring, render breathing more difficult, and consequently act as a potential cause of dyspnoea.

(E) Atmospheric Changes.

Under most exceptional circumstances, the atmosphere in the chamber one is living in may contain poisonous gases, or an undue amount of carbon dioxide, or a lack of oxygen, and consequently hyperpnoea would result. These are, however, very uncommon, and ordinarily there is a negligible amount of carbon dioxide in the air one breathes.

The oxygen content, however, is subject to considerable variation, depending on the altitude. To a person first arriving at a high altitude, hyperpnoea and anoxemia will result, and slight exertion will cause dyspnoea. Later on, certain compensatory processes occur and the dyspnoea rendered less likely. Nevertheless, at an altitude of fourteen thousand feet, the blood is at best only about 85 % saturated with oxygen and cyanosis is prevalent. The sequence of events is something as follows: The lowering of the oxygen tension causes a hyperpnoea, which results in a blowing off of carbon dioxide and an alkalosis. This prevents a further blowing off of carbon dioxide, and this reduces the ability of the blood to take on more oxygen. Hence anoxemia results despite hyperpnoea. Then, during the next few days, the excess alkalis are excreted by the kidneys and the normal carbonic acid to sodium bicarbonate ratio is restored, though with a lowered carbon dioxide combining power. A polycythemia also results in increasing the oxygen carrying capacity of the blood.

(F) Nervous Causes.

Not only may nervous upsets cause a real increase in demand for respiration, but certain people may be hyperconscious of their breathing. They may be aware of unusually small degrees of hyperpnoea. The people will usually promptly become frightened and fear that they are suffocating. The increased respiratory effort then resulting might cause real distress or dyspnoea. Due to some peculiar mental kink, they may be quite unable to utilize the true vital capacity of their lungs.

The respiratory center may become relatively inactive, due to fatigue, oedema, intracranial pressure, or some other disease process. Under such circumstances the patient might suffer from air hunger, show signs of anoxemia, cyanosis and acidosis, and yet there may be no corresponding hyperpnoea.

Treatment of Dyspnoea.

Dyspnoea is a symptom, resulting from widely varying causes, and adequate treatment will be correction of the causes acting in the individual case. A very brief schedule of various types of treatment to be used has been arranged by Means.

(1) Reduce the Metabolic Rate.

(a) Rest, giving freedom from unnecessary muscular exertion, is the most generally applicable and most effective factor. Sedatives to ensure freedom from pain and restlessness may be needed and should be given. Even the effort and anxiety of dyspnoea itself may raise the metabolic rate by 25%, or even 50 %, so that rest in bed with morphine may relieve the condition.

(b) Hyperpyrexia, Hyperthyroid-

ism and such specific causes of high metabolic rates, demand their own appropriate treatment.

(2) Improve the Action of the Blood.

(a) Increase the hemoglobin content in the anemias.

(b) Relieve any acidosis. For example, in diabetic ketosis, glucose and insulin are indicated. The giving of alkalis by mouth may give temporary relief.

(c) A circulatory failure is a common cause of dyspnoea, and the remedy here is to improve the blood flow. For example, digitalis or strophanthine to a sudden attack of fibrillation.

(3) Improve the Ventilation.

(a) The position of orthopnoea seems to allow the vital capacity to be utilized to its greatest extent. Make sure of an adequate airway.

(b) If there are signs of anoxemia, despite the hyperpnoea, oxygen may be of value.

(c) Bronchial spasm, if present, is well relieved by adrenalin.

(4) Stimulation of the Respiratory Center.

(a) There may be signs of anoxemia, and yet but little hyperpnoea, and no obvious reason in the chest to account for it. Carbon dioxide added to the inhaled air may stimulate the respirations and give proper oxygenation.

(b) Caffein is said to lower the threshold of the center to normal stimuli, and hence should be useful in morphine poisoning.

Appendicitis in Children.

By J. L. McDONALD, M.B.

The surgeons of the Hospital for Sick Children became deeply interested a few years ago in the prevalence of acute appendicitis in small children. Their interest was aroused following an extensive analysis of the histories of all patients admitted to the Hospital with this affection during the years 1922 and 1923. The facts that impressed us most in this analysis were: (1) that of the 122 cases admitted 91 or 74.6% had the appendix ruptured on admission, and (2) that while the mortality in the clean cases was nil—the mortality in the ruptured cases was 13, or 14.28%. In other words, the lives of 13 children had been lost, which might have been saved had the condition been recognized early and prompt surgical interference been carried out. The majority of the deaths appeared to be due to the overwhelming infection in those that occurred early or to the toxaemia of intestinal obstruction in those that occurred later.

In searching for the cause of the delay in treatment in these cases it was found that in a few the family physician had either failed to recognize the true nature of the case or—having recognized it—had treated it for some time along medical lines. In the vast majority, however, the blame could only be placed on the parents of the children. They apparently did not realize the dangers that might accompany acute abdominal pain, and had treated the children with home remedies—caster oil being the most favoured—for several days before consulting their doctor The subject was discussed at a meeting of the Surgical Section of the Academy, and an earnest hope expressed that the Physicians of this city would do all in their power to get these cases to the Surgeon early, and have them operated on before the appendix had ruptured We also hoped that we might be able to improve our method of dealing with the ruptured cases.

In 1927 the histories of patients ad-

mitted with appendicitis during the years 1924, 1925 and 1926 were carefully examined, and it was hoped that with the importance of early diagnosis being stressed—along with the new methods of treatment instituted in the ruptured cases—our mortality would show a definite drop. During this period 255 cases were admitted and, of this total 70, or 66.6%, had the appendix ruptured on admission, with a mortality rate among the ruptured cases of 11.8%. The mortality in the clean cases being nil, as before.

Following this analysis we were forced to admit two things: (1) that our results as regards early diagnosis and mortality rate had improved very little over the previous period, and (2) that patients submitted to secondary operations for the relief of intestinal obstruction and other complications almost invariably did badly.

Recently we have analysed the histories of patients admitted to the Hospital during the years 1927 and 1928. It was during this period that we recognized more than ever before the importance of giving large quantities of Saline to patients with appendicitis complicated by general peritonitis and intestinal obstruction, and we felt convinced by this means we had been able in this period to save the lives of some children who would have died in our earlier series. During this period 220 cases were admitted to the Hospital with acute appendicitis, and—of this number—126, or 57%, had the appendix ruptured on admission with a mortality among these ruptured cases of 14.28%. The mortality among the clean cases remaining nil. These findings were very disappointing and also very puzzling since, in spite of what we considered improved methods of treatment our mortality had actually increased. In searching for a possible explanation of this apparent discrepancy, we found that the percentage of children admitted under 5 years of age was almost twice as great as in the period of 1922 and 1923—the exact number being 46, or 21%, of the total admitted.

Taking this small group of 46 we found that 90% of them had the appendix ruptured on admission, followed by 11 deaths or a mortality of 24%. In other words 61% of all the deaths occurring in this period were in children under 5 years of age. It was this group that was swelling our mortality rate and it was a revelation that should not be passed over lightly because the majority of lay people, and indeed some physicians have the false idea that appendicitis does not occur in small children.

Here we have a group of small kiddies who apparently are liable to attacks of appendicitis just as older children are, but who, because of their age, have difficulty in making known their symptoms until the case is advanced, and the appendix ruptured with general peritonitis established. Moreover, it is very clear in our experience that these younger children offer less resistance to peritonitis than do older children.

From the facts enumerated above it appears fairly obvious that appendicitis is a common ailment of children at all ages. It is also quite evident that if recognized early and properly treated the outlook is not serious. On the other hand if it is allowed to progress until the appendix ruptures the result may be, and frequently is, disastrous.

I would like just here to briefly describe what we consider the important signs and symptoms to rely on in arriving at a diagnosis The most important symptom undoubtedly is pain —described by older children as being cramp-like in nature, and usually referred to the umbilicus. Younger children point vaguely to the central quadrant of the abdomen, pulling their knees up and screaming as if in pain. This pain is soon accompanied in many cases by nausea and vomiting. The most constant sign is local tenderness, which is elicited on palpating over the inflamed organ. This, as a rule, is situated in the right lower quadrant of the abdomen, but in the retro-caecal type, it is frequently felt far out in the flank,

and in the pelvic type may only be elicited on rectal examination. Increased temperature, raised white blood count, hyperaesthesia and abdominal rigidity should be taken for what they are worth, but their absence should not mislead one in making a diagnosis.

In closing let me emphasize the point that appendicitis is one of the common causes of acute abdominal pain in small children. Moreover, this fact must not alone be recognized by doctors, but by the parents of children. If we can succeed in teaching them the danger accompanying acute abdominal pain in a child, and have them early seek the counsel of their physician, we will have a distinct advance in lessening the mortality from this common malady.

Cyanosis of the New Born.

Part II.

Congenital Atelectasis and Thymic Enlargements.

By FRASER M. GREIG, M.D.

Congenital Atelectasis.

By congenital atelectasis is meant a failure of the whole or any considerable portion of the lungs of the new born to expand after birth. Thus there is a persistence of, or a return to the unexpanded foetal condition of the lung. Atelectasis is to a degree physiological during the first few days after birth, gradually disappearing with increasing strength. Two days probably elapse before all parts of the newborn's lungs are functioning. The volume increases rapidly during the first day only and in some cases several days pass before the physiological atelectasis passes off. The symptom producing atelectasis, however, must be much greater than any physiological atelectasis.

The foetal lungs tend to lie in the posterior parts of the pleural cavities, are small and compact and the diaphragm is very high. The first few respirations are brought about chiefly by the accessory respiratory muscles. The thoracic cage expands and the diaphragm descends from its high position. This is followed by expansion of the lungs. All parts of the lung, however, do not expand equally The posterior part of the lower lobes, the paravertebral portions and the portions around the hylus are the last to expand, and it is in these portions that the atelectasis is most persistent.

ETIOLOGY:

1. The condition is usually found in premature and feeble infants, but not necessarily so.

2. Atelectasis is the pathological condition with which asphyxia at birth is usually accociated. In most of the cases the atelectasis is overcome by the methods of resuscitation, in some, however, these means are only partially successful, so that an abnormal portion of the lung remains in the atelectalic state.

3. Many cases give no history of asphyxia at birth, but the initial respiration in these cases have not been of sufficient force and depth to cause normal pulmonary expansion.

4. Injury to the respiratory centre by cerebral hemorrhage or oedema.

5. In the premature the irritability of the respiratory centre is low, while in those suffering from asphyxia at birth it is lowered. It has also been suggested that the lack of muscular activity in the premature and feeble infants is responsible for diminished CO_2 content of the blood, and is thus indirectly a factor leading to the weakened action of the respiratory centre.

6. The poorly distended lungs may become more and more gradually collapsed owing to the weakness of the child and the yielding character of the thorax, which makes satisfactory respiration difficult or impossible, thus asphyxia develops as the result of atelectasis The actual cause of the cyanosis is probably not the collapsed condition of the lungs with the resultant decreased area of aeration, as cases are recorded where two-thirds of the lungs have been collapsed without cyanosis There are two factors that cause the cyanosis: (1) the collapsed lung, and (2) the rapid, shallow breathing of these infants

PATHOLOGY:

If the atelectasis be complete and the infant has never breathed, the lungs are dark red or blue red, small, very vascular, entirely collapsed, firm to touch, do not crepitate and sink in water They are capable of being forcibly inflated, thus distinguishing it from a pneumonic process If the child has breathed the atlectasis is usually found in the lower lobes posteriorly and around the hilus. The surfaces may be distended and the atelectasis present in the deeper portions. There is often a pneumonic process present, a condition to which these infants are very prone.

SIGNS AND SYMPTOMS:

The breathing is rapid, irregular and shallow and may be attended by evident retraction of the intercostal spaces and the lower portion of the thorax at the insertion of the diaphragm.

The temperature is usually persistently subnormal

The pulse is weak and slow.

The infant generally lies with the eyes closed, crying but little and never loudly and makes feeble if any efforts to suck.

Physical signs of the chest are often lacking.

On percussion there is usually resonance over the entire chest. The collapsed areas are surrounded by areas of overdistension and thus resonance is not much interfered with. If only one lung is involved a difference on the two sides may be detected.

On auscultation the breadth sounds are very feeble and the expiratory sound in particular may be nearly inaudible. Bronchial breathing is not found. Crepitant rales may be found, and if so, are usually best heard at the bases posteriorly.

Cyanosis is the most outstanding finding. This may be of all degrees and varies from time to time; it is usually not severe. It is not constantly present, but occurs in intermittent attacks. During an attack, if the child be made to cry the degree of cyanosis present will decrease. This is a very important feature of the cyanosis and the procedure should be carried out in all cases of unexplained cyanosis.

The infants may have convulsions and periods of apnoea.

X-Ray plates will be of use if available, not in showing anything in particular in the lung, but more by helping to rule out Congenital Heart Disease and Thymic Enlargements.

DIAGNOSIS:

The condition is usually found in premature and weaklings Many cases will have a history of asphyxia at birth. The cyanosis occurs intermittently. The attacks may be brought on by physical exertion and interference with respiration as in nursing. The child's cry is feeble, there is no elevation of temperature, but is more often subnormal, the respirations are rapid and shallow, the pulse slow and weak.

Atelectasis is to be differentiated from the other causes of cyanosis being discussed in this paper. It must also be distinguished from that occurring with lung infections. It must be remembered that there are occasional cases in which a child is born with pneumonia.

TREATMENT:

The treatment of atelectasis is much the same as that of Asphyxia Neonatorum. At birth if asphyxia is present

the child must be made to cry loudly and the breathing must be easy. These infants have a great tendency to relapse so that they must be stimulated to cry several times daily. This is best accomplished by gentle flicking of the skin. This must be kept up for several days even though the cyanosis has disappeared. During the attacks of cyanosis they should be made to cry and oxygen supplied at this time by means of nasal catheters is very useful.

The infants are usually weaklings or prematures, so that the general care of prematures must be carried out. The child's energy must be conserved and an attempt made to build them up as quickly as possible. They should be kept in a hot room of 75 to 95 degrees F. They usually have a subnormal temperature, and if this is the case they cannot assimilate their food properly. The heat-regulating centre is not functioning properly, so that their body temperature will fall with that of their surroundings, on this account the temperature of their environment should be kept almost up to body heat. Their caloric requirement is higher than normal infants. If very weak they should not be nursed, due to the energy that must be exerted. The milk in these cases should be administered by a premature feeder which allows the infant to receive its food with practically no loss of energy Breast milk should be used.

If the child is very weak and the temperature subnormal, it should not be bathed, for the sake of stimulation, as this is accomplished by loss of surface heat.

Drugs are of little value

PROGNOSIS:

This depends upon the degree of atelectasis, which in turn usually depends upon the degree of debility. If the attacks of asphyxia and cyanosis appear with frequency during the first two weeks of life the outlook is grave despite treatment. In favourable cases the attacks become less and less frequent and finally cease. Pneumonia in these cases is the worst complication and it is very liable to develop owing to their weakened condition and the hemorrhagic congested state of their atelectatic lungs.

Infants who have suffered from congenital atelectasis may remain in delicate health for a long time although they ultimately recover completely.

Thymic Enlargements

There is not one of the endocrine glands, if it may be considered as an endocrine gland, that has been so shrouded in mystery as the thymus. It has been described as either the sole cause or an associated cause of many pathological conditions. Each concept advanced as to its origin, gross and microscopic anatomy, function, growth and pathological significance has immediately been challenged. The result in the literature is chaos. Any of the above aspects would be a study in itself. This in a few words gives us some idea of what is not known of the thymus. Practically speaking, there is nothing universally accepted.

The lack of knowledge is not due to lack of research. A great deal of work has been done but it has not been conducted without source of error and many false conclusions have been drawn. It is not intended to discuss at all the condition of status lymphaticus but rather confine the study to the thymic enlargements seen in infants and young children without the association of status lymphaticus.

This condition receives many names and is variously known as Enlarged Thymus, Persistent Thymus, Hyperplastic Thymus, Thymic Asthma and Mors Thymica. The term Thymic Asthma originated with Kopp in 1829. The existence of the syndrome was denied by Friedeleben in 1858. Since this time there have been the two schools. But nevertheless, a sufficient number of cases of respiratory stridor occur from year to year to keep the concept before the eyes of the paediatrician and general practitioner.

Before going on to the clinical as-

pects and the various theories of production of the syndrome, it would be well to discuss briefly some of the more widely accepted views as to anatomy, physiology and growth.

Gross Morphology and Relations

The thymus is a soft white fusiform mass usually bi-lobed, but may be trilobed or conglomerate. Situated chiefly in the thorax it may extend cephalad into the neck region to a variable extent, usually not more than 2 cm. The fourth costal cartilage generally marks its caudal extremity but it has been known to extend to the diaphragm. Ventrally it is in relation with the sternum, the origins of the sterno thyroid muscles, sterno costal and sterno clavicular arteries and intermammary arteries. Dorsally it comes into contact with the aorta and superior vena cava and their branches, the pulmonary artery and the pericardium. It is bounded laterally by the pleural sacs and the phrenic nerves. The nerve supply is through the cervical sympathetic and vagus nerves.

Histology.

The lobes of the gland are divisible into primary and secondary lobules and in the latter, cortical and medullary portions may be distinguished. The cortex differs from the medulla in that it is densely filled with small cells, indistinguishable morphologically from lymphocytes. There are two views concerning their nature: (1) Epithelial in nature (2) Lymphocytes which have penetrated the organ and greatly changed its appearance. These small cells of the thymus possess the same basophilic cytoplasm, the same power of amoeboid movement and the same sensitivity to X-Rays as true lymphocytes. The compensatory hypertrophy of true lymphatic tissue following removal of the thymus as recorded by Basch is an interesting argument in favour of the lymphatic nature of the small cells, but requires confirmation. These small cells are placed in a reticulum; these reticulum cells may be recognized by their large pale staining nuclei, and are epithelial in origin. In the medulla the small cells are less abundant and for this reason the tissue stains less intensely. The reticulum cells are present in larger numbers. In the thymus clumps of cells are seen. These are called Hassal's Corpuscles and are formed through a clumping and degeneration (hyaline, fatty or colloidal) of the epithelial cells, or of the reticulum cells formed from them. The cells in the centres of these corpuscles are, judging from their appearance, either dead or very nearly so.

Size, Growth and Involution of the Thymus.

Hammar has done some very careful work recently on the growth and involution of the thymus. According to him there are four concepts of growth in the literature. (1) The thymus reaches its maximum size at birth and then atrophies. (2) It reaches its maximum at birth, remains stationary for from one to two years, and then atrophies. (3) It increases from birth to puberty and then atrophies. (4) The thymus entirely disappears sometime between the ages of one and twenty years.

Hammar has demonstrated that the confusion regarding the normal size of the gland is caused by failure to recognize the occurence of age involution beginning at puberty and "accidental involution" occurring in inanition or in any condition which causes loss of weight. By taking thymus glands from patients who died of adequate pathological causes within twenty-four hours of the onset of illness, he has established new normal standards for thymic weight for given age groups. Begining with an average weight of 13 grams at birth, the thymus increases to an average weight of 35 grams at puberty, then atrophies to 15 grams by the age of fifty. Scammon of the University of Minnesota, using the same criterion, has increased the number of cases to 1074. He has also compared the resultant growth curve of the thymus to that of

the mesenteric lymph nodes. The two are parallel. Only the lymphoid tissue and the thymus have this type of post natal growth curve. Therefore, as far as weight is concerned, the thymus acts as a lymphoid organ.

The involutionary changes are briefly as follows:— The colour of the tissue becomes grey and finally yellowish owing to the increase in the amount of connective tissue and fat and decreased vascularity. The microscopical changes of age involution consist of a loss of the lymphocyte-like cells, changes in the reticulum cells and infiltration of fat and connective tissue. This form of involution has been demonstrated experimentally in chronic and in acute inanition in rats. Jonson found a reduction of about 80 per cent. in the cortex of these animals after four days of acute inanition. Hammar notes another interesting point, that following diseases such as influenza there is an involution similar to that of inanition, even though the body is still well nourished. Experimentally the X-Rays cause a reduction of lymphocytes in the cortex, thus reducing the size of the gland.

Function of the Thymus.

As previously stated, the entire function of the thymus is not understood. The literature as a whole affords little or no reliable evidence that the thymus has any true endocrine function. However, the fact that an internal secretion has not been isolated is not proof that no secretion exists.

Friedelben in 1858 experimented with eighteen animals. Dogs and other animals were used, but his results are true only for the dogs, as the other animals were open to experimental error. In some he removed the thymus alone and in others he removed the thymus plus the spleen. He concluded that the thymus is not essential to life, but that loss of spleen and thymus together is necessarily fatal. However, the chief significance of his experiments is the demonstration that thymus extirpation is feasible in dogs at least.

In all probability the organ is of significance in the physiological and pathological processes merely by virtue of its lymphoid character. It is probably concerned with defensive mechanisms against infections. As previously stated, Hammar noted an involution following diseases such as influenza similar to that involution seen in inanimation. This defensive mechanism of the thymus has been seen also at the Sick Children's Hospital and reported by Brown, Morgan and Rolph. In two cases of enlarged thymus the children had mild upper respiratory infections following X-Ray therapy which is known to produce involution, the respiratory infections became much worse and finally caused death. The fact that the thymus involutes after the age of common infections shows that it probably acts as a defensive mechanism against infection and then when it is no longer required, it undergoes involution

Etiology and Theories of Production of Symptoms.

If one accepts the physiology of the thymus, viz., that it acts as a defensive mechanism in infants and young children, one may consider thymic enlargements as secondary to some primary infection, intoxication or disturbance of metabolism. The enlarged thymus may be present as an anomaly or in some cases it may be due to an acute congestion caused by an acute infection, similar to that produced in the spleen in the course of an acute infection.

Some absolutely deny that an enlarged thymus in infancy can produce the symptoms attributed to it. The therapeutic test is almost convincing. It is known experimentally that X-Rays will cause involution of the gland. A child with the symptoms of enlarged thymus and who on X-Ray study is shown to have an enlarged shadow in the area of the great vessels, after ruling out other possible causes of the symptoms, is diagnosed as a case of enlarged thymus. X-Ray therapy is carried out; after a few treatments the

shadow has returned to its normal size and the symptoms have disappeared. This is almost conclusive that the thymus is capable of producing these symptoms. There is only one way in which the test is not completely foolproof. Might the symptoms not be relieved by the action of the X-Ray on other tissues which it penetrates in the region of the thymus, for example, skin, bone or muscle tissue? This is a very remote possibility, but not a very great probability. The cases presented are in too grave danger to try this non-specific action of the X-Ray on other parts of the body so that there has not been any confirmation or denying of this possibility.

Those who disclaim the thymus as the cause of the symptoms do so chiefly on the ground that they cannot perceive of the thymus being capable of producing such profound symptoms by pressure in the mediastinum. They believe that the enlargement of the gland is physically not capable of producing sufficient pressure on surrounding structures to produce the symptoms attributed to enlargement of the thymus. The great majority disclaim it on the mechanical basis.

This brings us to the question of how the gland produces the symptoms. There are three main theories or schools at present. Which of these is responsible, at present, it is impossible to state. There is also the possibility that they may act in combination. These three theories are:

1. The Pressure or Mechanical Theory.
2. The Internal Secretion Theory.
3. The Anaphylactic Theory.

1. The Pressure Theory.—There are several possibilities of how pressure in this area may act. It may act on the trachea, on the great vessels, on the vagus nerve or the recurrent laryngeal nerve. Part of an article by Boyd, who has done considerable work on the Thymus, shall be quoted.

"In my necropsy records since 1915, there has not been a single case in which pressure on the trachea by the thymus could be interpreted as the cause of death. In explaining the mechanical production of symptoms by the thymus it is necessary to have in mind the following points: (a) The normal increase in the size of the structure. (b) Changes in shape and position during the first two weeks of life, due to expansion of the lungs. (c) rapid rate of growth of the chest as compared with the growth of the thymus in infancy.

The variability in size and shape of the thymus has long been recognized. Noback showed that the normal foetal thymus is broad and is changed to an elongated type by respiration. This process takes about two weeks, following birth. Noback demonstrated by transverse sections of the body that the expanding lungs force the thymus posteriorly into the mediastinum and laterally and inferiorly around the heart so that parts of the gland may extend backward to the trachea and vertebral column and downward to the diaphragm."

Boyd found a loss of weight in the thymus of from 5 to 8 grams from the mean birth weight of 13 grams during the first two weeks of life. By six weeks the gland averages 17 grams. Since there are few deaths of well-nourished children during the first month of life, the material is not adequate as yet to establish the age at which the thymus regains its birth weight. There is some evidence to show that this process parallels the normal loss in body weight and recovery within the first ten to fourteen days.

Putting these observations together gives the following process. During this period while the thymus in the new born child is being compressed around and between the mediastinal structures, it is also losing weight. After this process is well under way or is complete the gland begins to increase in size, so that the portions of the thymus around and between the blood vessels and trachea may grow suffi-

ciently to cause pressure on the vessels and nerves, particularly on the recurrent laryngeal nerve. There are two clinical observations which support such an hypothesis: (1) Most infants do not develop thymic symptoms during the period of loss of weight of the gland. (2) Most infants frequently have along with an inspiratory stridor, hoarseness and a crowing cry suggestive of spasm of the vocal cords from irritation of the recurrent laryngeal nerve. Blackfan noted that this cry sounded like the brassy voice of a man with an aortic aneurysm.

If the pressure theory is true, it seems most likely that the symptoms are produced by pressure on the recurrent laryngeal nerve and the veins, as it seems almost impossible to conceive of great enough pressure developing to materially interfere with the trachea of the arteries.

2. The Internal Secretion Theory.—As pointed out before, there has been no definite proof that the gland has any true internal secretion. This does not, however, prove that there is not one. If a secretion is responsible for the symptoms, it must act centrally as a toxic agent on the respiratory centre and other vital centres. In support of this theory is the fact that some cases with symptoms show no enlargement and vice versa, and that these cases improve after treatment, also the fact that recurrence of enlargement occurs without recurrence of symptoms.

3. The Anaphylactic Theory.—This theory states that the body becomes sensitized by a specific nucleo protein formed from the lymphocytes in the thymus as a result of necrosis. The tissues on subsequent injury may give rise to free antigen, thus causing an anaphylactic reaction. J. J. Vas reports that X-Ray plates of children with exudative diathesis were compared with a group of control cases. It was found that those with exudative diathesis showed a wider shadow in the region of the thymus gland than the control cases. This, of course, is not much evidence.

The manner of production of symptoms is not understood. From the evidence available it would appear that pressure is the most likely cause, especially that on the recurrent laryngeal nerve and the great veins at the base of the heart.

There is no sex incidence in this condition.

Signs and Symptoms.

A somewhat typical case history may be cited: A male infant twelve pounds in weight was seen one hour after birth. The labour had been easy, but with the first cry the obstetrician had noticed that the child's breathing was decidedly abnormal. The patient presented the most unusual appearance. The skin, lips and nails were intensely cyanotic and the inspiratory stridor was distinctly audible in the adjoining room, while the epigastric retraction was equal to that accompanying the severest form of laryngeal diptheria. Percussion and X-Ray both detected the presence of a thymus filling nearly half of the chest cavity. Radium was applied and within forty-eight hours the baby showed decided improvement which continued until at the end of a week he was nearly normal in appearance.

X-Ray plates two and ten weeks after the treatment showed a normal thymic outline. Fifteen months after discharge the child was still well

On physical examination one might detect an increased width of the mediastinal dullness over the region of the thymus. Epigastric retraction might also be found.

The symptoms are variable and all symptoms ascribed to enlargement of the thymus are not present in one case. The majority of the cases will present only one of the following suggestive symptoms, but a few will present two or more:

1. Cyanosis.—This may occur alone or be associated with Breath Holding Spasms. In the greater number of cases this is not present from birth, but occurs some hours or days after birth.

The cyanosis is usually not persistent, may be mild and associated with suffocative attacks of a minute's duration.

2. Breath Holding Spasms.—This is the most common symptom. The child suddenly holds its breath for a short period and becomes cyanotic. These attacks usually occur during a crying bout and may be accompanied by a transient loss of consciousness. The spasms may occur several times in one day or be quite infrequent.

3. Syncope.—These attacks of loss of consciousness may occur apart from the Breath Holding Spasms.

4. Cough.—The cough is hoarse or brassy and may be continuous or intermittent.

5. Choking Attacks.—These usually occur while nursing are of short duration and accompanied by cyanosis.

6. Noisy Nasal Breathing.

7. Asthmatic Attacks, differing from the usual asthmatic attack in that the difficulty is in inspiration and not in expiration.

The above symptomatology has been presented by Brown, Morgan and Rolph. In their series of cases, cyanosis is the most common finding either occurring along or with one of the other symptoms. Breath Holding Spasms were present in over 50 per cent of their cases. They also draw attention to symptoms which have been previously overlooked, but which showed improvement following X-Ray therapy. These are nervous manifestations: sleeplessness, restlessness, irritability and rapid panting breathing.

Diagnosis.

The diagnosis is made by the demonstration of an enlarged thymus either radiologically or by physical examination. Without this enlargement of the thymus, one cannot and should not definitely diagnose the condition. One must remember that all of the manifestations of an enlarged thymus may be produced by other causes, many of these causes being more likely to produce the symptoms than an enlarged thymus. One must be very guarded in making a diagnosis and must absolutely rule out all other causes of the symptoms. A great deal of the criticism that has fallen upon the thymus has been due to not adopting this conservative attitude Cases are on record of prolonged radiation treatment of perfectly apparent cases of cerebral haemorrhage and congenital heart disease. Of course if unable to make a definite diagnosis in urgent cases and the thymus is suspected, one is justified in submitting the infant to the therapeutic test. However, if no improvement follows two or three treatments, it should be concluded that the diagnosis is wrong.

While the X-Ray will make the diagnosis in the great majority of cases there are a few cases in which it fails. A few cases will not show an enlargement of the thymic shadow although the infants have definite manifestations. These cases may be accounted for by one of the following: (1) The enlargement may occur in an antero-posterior direction and would therefore not show in plates taken in the antero-posterior position. These cases may occur, but must be very few. (2) Girstenberger has been able to show in the same child and at the same sitting an enlarged shadow and a normal shadow in the region of the thymus. Viewing this under a fluoroscope, he noted that the normal shadow could be replaced by one of normal size if the patient took a deep inspiration. Similarly the abnormal shadow was markedly increased by deeply and forcefully expiring. (3) If one accepts the toxic theory, the size of the gland would have no definite relation to the severity of symptoms.

Apart from these fallacies, the X-Ray plate will show the enlargement. True antero posterior enlargement is rare and the normal shadows do not occur with ordinary respiration.

The symptoms are usually not present from birth.

Differential Diagnosis.

The condition must be differentiated from the other forms of cyanosis being discussed in this article. These are chiefly Cerebral Haemorrhage, Congenital Atelectasis, Congenital Heart Disease and Infections. The main points of differentiation may be stated briefly.

Cerebral Haemorrhage.—The child is restless and may have evident sensory and motor disturbances The fontanels may bulge, the cyanosis is usually continuous and is present from birth. The history of the labour will be helpful. Lumbar puncture will usually confirm the diagnosis, the cerebro spinal fluid may be blood-tinged or yellowish due to haemolysis of the red blood corpuscles.

Congenital Atelectasis.—This is usually seen in premature and debilitated infants. The cyanosis is present from birth and intermittent in character. If the child be made to cry during an attack of cyanosis, the degree of cyanosis lessens.

Congenital Heart Disease.—There may or may not be a heart murmur, the cyanosis is usually constant, present from birth and increased by crying. The heart is nearly always enlarged, particularly to the right side. The red blood count is usually high.

Infection, Especially Pneumonia.—It must be remembered that there are occasional cases in which the child is born with pneumonia. The temperature will be elevated and the child is toxic in appearance. The cyanosis is usually not intermittent and not decreased by crying. In the pneumonias, bronchial breathing and adventitious sounds will be detected and some evidence of impaired resonance.

Thymic Enlargements.—These symptoms have been discussed; they are usually not present at birth, but may occur in hours, days or weeks after. The attacks are intermittent. X-Ray plates or the fluoroscope will usually show an enlarged thymic gland.

In the new born there are not many conditions that would give the laryngeal symptoms, but one should think of laryngeal diphtheria, and in older infants and children spasmodic croup, intantile tetany and other tumors of the chest and bronchial glands. Cough and choking will be produced by many more common causes such as local irritations and swallowing.

Treatment

The recognized treatment is that of X-Ray therapy. A few of the larger obstetrical institutions are carrying out routine Roentgen-ray examination of the chest. In these institutions it is found that almost 50 per cent. of the infants show an enlarged thymic shadow. Of course a very small percentage of these develop symptoms. The general attitude is against any therapy being carried out in cases showing merely enlargement, and to be on the lookout for a symptom, at which time therapy may be started. That is, prophylactic treatment should not be carried out merely in the presence of an enlarged gland.

The detail of X-Ray therapy varies and shall not be discussed. The initial treatment is usually given, followed by the second treatment in one week's time, the third in twelve more days, and fourth in another week. The symptoms usually disappear rapidly, and after the third treatment the gland is usually reduced in size. The fourth treatment is given to guard against recurrences.

Prognosis.

1. The mortality of this condition is not known, as in many cases it is not diagnosed.

2. Following treatment the symptoms are either relieved complete or greatly improved.

3. Following treatment there is marked improvement in general health.

4. About 20 per cent. of cases show recurrence of either symptoms or enlargement. These usually remain normal after a second course of treatment.

5. As far as is known at present, there are no ill effects produced by

treatment except occasional vomiting or anorexia for twenty-four hours after.

6. The changes which some claim are going to occur at puberty are not known at present. However, accidental involution has always occurred following inanition as shown by Hammar with apparently no demonstrable change.

Summary.

1. The function of the thymus is not understood. There is good evidence that it acts as a lymphoid organ and defense mechanism against infections.

2. It would appear from clinical studies and the results of X-Ray therapy that the disturbances attributed to the thymus are justly attributed to it.

3. The manner of production of the symptoms is not settled. The theory of pressure is probably the most widely accepted at present, and especially pressure on the vessels and recurrent laryngeal nerve.

4. The diagnosis should be made only after ruling out all other causes and finding an enlarged thymus.

5. A few cases show no enlargement. In these cases if no other cause can be demonstrated, one is justified in carrying out the therapeutic test.

6. X-Ray therapy is the recognized treatment.

7. In cases failing to respond to X-Ray therapy, other causes should be sought for.

8. As far as we know at present there are no ill effects produced by treatment, but many beneficial results.

9. A few cases will show recurrences, but these usually respond after a second course of treatment.

Shakespeare on Syphilis

From Timon of Athens, Act IV., Scene III.

Timon (to the two courtesans): "Consumptions sow
In hollow bones of man; strike their sharp shins,
And mar men's spurring. brack the lawyer's voice,
That he may never more false title plead,
Nor sound his quillets shrilly: hoar the flamen,
That scolds against the quality of flesh,
And not believes himself: down with the nose,
Down with it flat; take the bridge quite away
Of him that, his particular to foresee,
Smells from the general weal; make curl'd-pate ruffians bald;
And let the unscarr'd braggarts of the war
Derive some pain from you: plague all;
That your activity may defeat and quell
The source of all erection."

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